REMARKS

A check for the fees for a one month extension of time accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of time is needed, this paper is to be considered such Petition, and any fee charged to Deposit Account No. 06-1050.

Claims 1-23, 25-37, 49-54, 93-95, 99-102 are pending in this application Claims 1, 11 17, 18, 21-23, 34 and 35 are amended Claim 1 is amended for clarity. The claim is directed to a combination of two collections. As amended, the claim clearly recites that the combination contains two collections: a collection of capture agents, and a collection of oligonucleotides. The capture agents specifically bind to preselected polypeptides (they are not bound to the recited preselected polypeptides, but possess specificity for the preselected polypeptides). The oligonucleotides *encode the preselected polypeptides* to which the capture agents possess specificity. The collection of capture agents contains at least 10 sets of capture agents, where each set is specific for a different preselected polypeptide E_m. The collection of oligonucleotides encodes at least 10 different preselected polypeptides. Claims 11, 17, 18, 21-23, 34 and 35 are amended herein to correct obvious errors, for clarity and for consistency with claim Claims 100-102 are added. Basis for claim 100 can be found, for example, at page 13, lines 15-23. Claims 101 is original claim 10. Claim 102 finds particular basis in the specification as originally filed. For example, basis can be found in original claim 10 and in the specification at page 6, line 30, - page 7, line 2. No new matter is added.

Claims 10 and 37 are not rejected over any cited art. Hence it appears that claims 10 and 37 are considered to be free of the art of record.

THE REJECTION OF CLAIMS 1-23, 25-37, 49-54, 93-95 and 99 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 1-23, 25-37, 49-54, 93-95 and 99 are rejected under 35 U.S.C. §112, second paragraph, for the reasons enumerated and addressed below. Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks.

Claim 1 is rejected as being indefinite in the recitation of "set of capture agents" because there is insufficient antecedent basis for this language. It is respectfully submitted that amendment of claim 1 herein has obviated this ground of rejection. As amended claim 1,

in (i) recites "the collection of capture agents comprises sets," thereby providing antecedent for subsequent recitation of "set" elsewhere in the claim.

Claim 11 is rejected as being indefinite in the recitation of "a polypeptide-encoding region" because claim 1 fails to provide antecedent therefor. It is respectfully submitted that amendment of claim 1 herein has obviated this ground of rejection. As amended claim 1 provides antecedent for this language. Claim 11 also is amended to recite language consistent with claim 1.

Claim 23 is rejected as indefinite in the recitation of "polypeptide-encoding region to which a capture [agent] binds." Claim 23 is amended to recite "polypeptide-encoding region (Em)," thereby rendering it clear that the component elements of the oligonucleotides are recited.

Claims 23, 34 and 35 are rejected as indefinite in the recitation of "polypeptide-encoding region to which a capture agent binds" because the capture agents bind to encoded polypeptides not to nucleic acid. Each of these claims are amended to render it clear that the claim is describing the component elements of the oligonucleotides.

THE REJECTION OF CLAIMS UNDER 35 U.S.C §102(b)

RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In re Spada, 15 USPQ2d 1655 (Fed. Cir, 1990), In re Bond, 15 USPQ 1566 (Fed. Cir. 1990), Soundscriber Corp. v. U.S., 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), cert. denied, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention." In re Lang, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). It is incumbent on an Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co., 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

"Rejections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the "'prior art'" . . .the [r]eference must clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the

compound without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings in the cited references. Such picking and choosing may be entirely proper when making a rejection of a §103, obviousness rejection, where the applicant must be afforded an opportunity to rebut with objective evidence any inference of obviousness which may arise from the similarity of the subject matter which he claims to the prior art, but it has no place in the making of a §102, anticipation rejection." (Emphasis in original). In re Arkey, Eardly, and Long, 455 F.2d 586, 172 USPQ 524 (CCPA, 1972).

Claims 1-9, 11-23, 25-36, 93 and 94

Claims 1-9, 11-23, 25-36, 93 and 94 are rejected under 35 U.S.C. §102(b) as being anticipated by Lerner *et al.*. (U.S. Patent No. 5,573,905) because Lerner *et al.* discloses an encoded combinatorial library in which each composition in the library includes a chemical polymer linked to an identifier oligonucleotide. The Examiner urges that:

> The binding reaction complexes (refers to instant claimed combination) are produced by the binding interaction between the chemical polymer of the library and a biologically active molecule (refers to instant claimed capture agent) wherein the binding interaction includes interaction such as antibodies to antibodies . . . (page 6 of the Office Action).

This rejection is respectfully traversed.

THE CLAIMS

Independent claim 1 is directed to a combination that contains **two collections.** The first collection is a collection of capture agents in which each capture agent specifically binds to a preselected polypeptide. The second collection contains oligonucleotides contain a region E_m that encode the preselected polypeptides to which the capture agents bind. The capture compound collection contains at least M members; and the oligonucleotide collection contains at least "m" members. Each E_m is unique in the oligonucleotide collection. The collection of oligonucleotides encodes at least 10 different preselected polypeptides The collection of capture agents contains at least 10 sets of capture agents, where each set is specific for a different preselected polypeptide Em. . Dependent claims specify particulars regarding the combinations.

The claims are *not* directed to complexes formed between the oligonucleotides and the capture agents. The combination contain *two collections*. As defined in the specification, a combination refers to two or more elements that are associated. In this

instance, the collections are associated because the oligonucleotides encode the preselected polypeptides to which the capture agents specifically bind.

Differences between the disclosure of Lerner *et al.* and the instant claims

Lerner *et al.* discloses combinatorial libraries in which each member of the library is tagged with a nucleic acid molecule that by virtue of its sequence identifies the library member to which it is linked. This is achieved by parallel synthesis of the library member and the nucleic acid in which each nucleotide is a code for a particular chemical unit in the library member. This library of oligonucleotide-tagged compounds is screened with "preselected biological molecules of interest." Molecules from the library that bind are identified by virtue of their tag.

The oligonucleotide tags disclosed by Lerner *et al.* do not encode the preselected biological molecules nor do they encode preselected polypeptides to which the compounds bind. Furthermore, Lerner *et al.* does not disclose a combination of two collections. The combinatorial libraries disclosed by Lerner *et al.* bear no resemblance to the instantly claimed combinations nor to member collections..

Analysis

As noted above, the products disclosed in Lerner *et al.* differs from the instantly claimed combinations in a variety of elements. Among them are that Lerner *et al.* does not disclose a combination of two collections, does not disclose a collection of capture agents that binds to preselected polypeptides nor a collection of oligonucleotides that encode the preselected *polypeptides* to which the capture agents bind. The oligonucleotides of Lerner *et al.* are not designed to encode polypeptides, but rather their respective sequences are codes that identify the members of the combinatorial library to which each is linked. The oligonucleotides are linked to the library members; they do not encode polypeptides to which the "preselected biological molecules of interest" bing.

The Examiner states that the compositions (the members of the combinatorial library), which he urges is the instantly claimed collection of oligonucleotides, includes identifier nucleotides, a linker and a chemical polymer. The identifier includes a coding region, which the Examiner urges is instantly claimed E_m. Without conceding the propriety of this characterization, the so-called E_m of Lerner *et al.* does not encode a polypeptide; it is an identifier that identifies the chemical polymer to which it is linked. It does not encode the chemical polymer nor does it encode a polyeptide that a) that is unique among the collection, and b) is preselected to bind to capture compounds. Further the nucleic-acid tagged chemical

polymer members of the libraries of Lerner *et al.* form a complex with a preselected biological molecule of interest (against which the library is screened) **not with polypeptides encoded by E_m.** The Examiner so-states. These elements are very different from the instantly claimed combinations.

Since anticipation requires that a reference disclose every element of a claim, Lerner *et al.*, which does not disclose a combination containing a collection of capture agents and a collection of oligonucleotides that encodes the polypeptides to which the captures agents bind, does not anticipate any of the rejected claims nor any of the presently pending claims.

Claims 1, 2, 11, 12, 25, 26, 36, 49-51 and 99

Claims 1, 2, 11, 12, 25, 26, 36, 49-51 and 99 are rejected under 35 U.S.C. §102(b) as being anticipated by Dower *et al.* (U.S. Patent No. 5,639,603) because Dower *et al.* discloses synthetic chemical libraries, which the Examiner urges correspond to the oligonucleotides of the instant claims, and binding reaction complexes. The Examiner states that the encoded synthetic libraries "comprise beads, identifier tags, and oligomers" and that the identifier tags are oligonucleotides that include "monomer specific information/coding site." This rejection is respectfully traversed.

Differences between the disclosure of Dower *et al.* and the instant claims

Dower *et al.* discloses methods for tagging the products of combinatorial chemical syntheses to produce encoded synthetic libraries. The combinatorial products are tagged with identifiers that are distinguishable. The identifier tags are used to track the synthesis of the members of the combinatorial library and serve to identify the member to which each is linked. The identifier tag can be an oligonucleotide in which the sequence identifies the reaction steps (*i.e.,* each base, or sequence thereof, indicates that a particular reaction was employed), and hence the resulting molecule. The oligonucleotide tags, as with Lerner *et al.*, are used to encode information regarding the structure of the linked combinatorial library member. The oligonucleotides *do not* encode preselected polypeptides, nor do they encode the combinatorial library members to which they are attached, nor do they encode polypeptides to which they are linked, nor do they encode polypeptides to which capture agents, such as antibodies, bind. Capture agents in the method are used to screen the combinatorial library members, not something encoded by the tag. Dower *et al.* does not disclose a combination that contains two collections: (a) a collection of capture compounds that bind to preselected polypetides; and (b) a collection of oligonucleotides that encode the preselected polypeptides.

Analysis

As noted, Dower *et al.* fails to disclose a combination that contains two collections: (a) a collection of capture compounds that bind to preselected polypetides; and (b) a collection of oligonucleotides that encode the preselected polypeptides. Further, if the oligonucleotides of Dower *et al.* correspond to the oligonucleotides in the instant claims as urged by the Examiner, then they differ from oligonucleotides of the instant claims because they are encoded with information regarding sequence steps that produced the library member to which each is bound; they do not encode polypeptides to which a collection capture agents (which the Examiner urges are the capture agents used to screen the combinatorial library) bind. The so-called capture agents as disclosed in Dower *et al.* bind to combinatorial library members, not to polypeptides that are encoded by the oligonucleotides linked to the combinatorial library members. In the instant claims, the capture agents are specific for polypeptides encoded by the oligonucleotides, not for members of a combinatorial library that are linked to the oligonucleotides. Therefore, because Dower *et al.* fails to disclose numerous elements of the instant claims, it does not anticpate any of the instant claims.

THE REJECTION OF CLAIMS 1-9, 11-23, 25-36, 49-54 AND 93-95 UNDER 35 U.S.C. §103(a)

Relevant Law

In order to set forth a prima facie case of obviousness under 35 U.S.C. § 103: (1) there must be some teaching, suggestion or incentive supporting the combination of cited references to produce the claimed invention (ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)) and (2) the combination of the cited references must actually teach or suggest the claimed invention. Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. Ex parte Gerlach, 212 USPQ 471 (Bd. APP. 1980). Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), but it cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination (ACS Hosp. Systems, Inc. v Montefiore Hosp. 732 F.2d 1572, 1577. 221 USPQ 329, 933 (Fed. Cir. 1984)). "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the

insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983). The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); see, also, In re Papesh, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963).

Claims 1-9, 11-23, 25-36, 49-51 and 93-95

Claims 1-9, 11-23, 25-36, 49-51 and 93-95 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lerner *et al.* and Dower *et al.* because Lerner *et al.* teaches a combinatorial library that contains compositions that include a chemical polymer and an identifier oligonucleotide that defines the structure of the chemical polymer, and the binding complexes. The identifier oligonucleotide includes a "coding region" that identifies the structure of the linked chemical polymer. The oligonucleotide tagged combinatorial library member chemical polymers are screened by binding to biologically active molecules, such as antibodies, which can be affixed to a solid support. The Examiner urges that the only difference between the teachings of Lerner *et al.* and the instant claims is that Lerner *et al.* fails to teach a computer system with software for analyzing the results of sorting. The Examiner urges that Dower *et al.* provides such teaching. This rejection is respectfully traversed.

The claims

The claims are discussed above

The cited references

The teachings of each of Lerner *et al.* and Dower *et al.* are discussed above

Analysis

The Examiner has failed to set forth a *prima facie* case of obviousness because the combination of teachings of the cited references does not result in the instantly claimed combinations and systems. The combination of teachings of Lerner *et al.* with those of Dower *et al.* does not result in the instantly claimed combinations and systems. As discussed above, neither Lerner *et al.* nor Dower *et al.* teaches or suggests a combination that contains two collections where one collection is a collection of capture agents that bind to preselected polypeptides and the other is a collection of oligonucleotides that encode the polypeptides to which the capture agents bind. Each of Lerner *et al.* and Dower *et al.* teaches oligo-nucleotide-tagged combinatorial libraries in which the sequence of the oligonucleotide

provides information regarding the structure of library member to which it is linked, and any "capture agents" (the preselected molecules for screening a library) are used to screen the combinatorial library.

The instant claims require that members of the collection of capture agents are specific for polypeptides encoded by the collection of oligonucleotides. The oligonucleotides described in either or both of the cited references do not encode the encode the library members nor do they encode any polypeptides to which the "capture agents" can bind. There is no teaching or suggestion in either reference to modify the oligonucleotides so that they encode polypeptides to which apture agents binds. The capture agents are used to screen the library members, not polypeptides encoded by the oligonucleotides. Neither reference, singly or in combination, teaches a combination that contains two collections as instantly claimed. Thus, the teachings of combined teachings of Lerner *et al.* and Dower *et al.* are deficient in failing to teach these requisite elements, as well as others, of the instant claims. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness.

Claims 1-9, 11-23, 25-36, 49-54 and 93-95

Claims 1-9, 11-23, 25-36, 49-54 and 93-95 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lerner *et al.* and Iris *et al.* (U.S. Patent No. 6,403,309) because Lerner *et al.* teaches a combinatorial library that contains compositions that include a chemical polymer and an identifier oligonucleotide that defines the structure of the chemical polymer, and the binding complexes. The identifier oligonucleotide includes a "coding region" that **identifies** the structure of the linked chemical polymer. The oligonucleotide tagged combinatorial library member chemical polymers are screened by binding to biologically active molecules, such as antibodies, which can be affixed to a solid support. The Examiner urges that the only difference between the teachings of Lerner *et al.* and the instant claims is that Lerner *et al.* fails to teach a computer system with software for analyzing the results of sorting. The Examiner urges that Iris *et al.* teaches an array of antibody that capture oligonucleotide probes labelled with peptide tags and also teaches a solid phase surface that comprises a plurality of loci. Each locus contains an antibody to one or more of the peptides of the peptide labelled oligonucleotide probes. The antibodies of the array specifically bind to the peptides. Further, it is alleged that the oligonucleotide probes may be first hybridized to target DNA before being captured by the addressable antibody arrays. The Examiner urges that Iris *et al.* also teaches an array that includes a computer

system so that it would have been obvious to one of ordinary skill in the art to have included a computer system in the products of Lerner *et al.* . This rejection is respectfully traversed.

CLAIMS

See above

ANALYSIS

Differences between the teachings of the cited references and the instant claims

Lerner *et al.*

Lerner *et al.* is discussed above. As noted, the oligonucleotides taught by Lerner *et al.* do not encode the linked polymer, nor does Lerner *et al.* teach combinations that contain *two* collections: a collection of capture molecules that specifically bind to preselected polypeptides (they are not *specifically bound to preselected polypeptides)*; and a second collection, a collection of oligonucleotides that encode the prepselected polypeptides.

Iris *et al*,

Iris *et al.* does not cure the deficiencies in the teachings of Lerner e*et al.* Iris *et al.* teaches polypeptide labels used in nucleic acid screening, such as for genotype mapping and gene expression analysis. The polypeptides taught by Iris *et al.* are chemically linked to oligonucleotides; the oligonucleotides do *not* encoded the linked polypetides. The oligonucleotides hybridize with nucleic acid molecules in solution. Antibody arrays bind to the peptide-olionucleotide-nucleic acid molecule complexes. The oligonucleotides *do not* encode polypeptides to which the antibody arrays bind.

The claims

As noted above, claim 1 and claims dependent thereon are directed to combinations that contain at least two collections: a collection of capture agents that bind to preselected polypeptides, and a collection of oligonucleotides that encode the preselected polypeptides to which the capture agents bind.

Analysis

As discussed above, Lerner *et al.* fails to teach a combination of two collections, fails to disclose oligonucleotides that encode the preselected polypeptides to which the capture agents specifically bind, and fails to teach other other elements of claim 1 and all dependent claims. Iris *et al.* does not cure these deficiencies. Iris *et al.* teaches arrays of antibodies and oligonucleotide probes. Iris *et al.* does not teach oligonucleotides that encode polypeptides to which the capture agents bind. First, the oligonucleotides described by Iris *et al.* are hybridization probes that hybridize with other nucleic acid molecules (column 7, line 65-

column 8, line 2). Second, the oligonucleotides do not encode polypeptides to which the antibodies of the array bind. The oligonucleotides are chemically attached to peptide tags and *it is the peptide tags* to which the antibodies bind; the oligonucleotides do not encode the peptides tags. Third, Iris *et al.* does not teach any oligonucleotides that encode the peptide tags. Thus, Iris *et al.* does not teach any oligonucleotides that *encode* a polypeptide to which the antibodies bind. Therefore, Iris *et al.* does not teach any elements that Lerner *et al.* fails to teach.

Additionally, neither Iris *et al.* nor Lerner *et al.*, singly nor in any combination of thereof, teaches or suggests other features of the claimed combinations, such as the elements that the collection of capture agents contain M members, which is the number of different polypeptides encoded by the oligonucleotides for which capture agents in the collection are specific. Neither Iris *et al.* nor any combination with the teachings of Lerner *et al.* teaches or suggests a relationship between the number of antibodies in any array and the number of different oligonucleotides.

Further, Iris *et al.* also does not teach all sets of capture agents specifically bind to different polypeptides encoded by the oligonucleotides nor that each set is specific for the same polypeptide. Iris *et al.* does not teach that each antibody in its array must bind to a different to a different polypeptide. In fact, Iris *et al.* states that the peptide-labeled oligonucleotides bind to one or more antibodies of the array (sentence spanning columns 5-6) and that each locus can bind to one or more peptides (col. 6, lines 10-15). Thus, Iris *et al.* does not disclose arrays where all sets of antibodies binds to different peptides.

The Office Action urges that column 21, lines 29-39 of Iris *et al.* describes peptide tags that are specific for the antibodies of the array. This paragraph states only that "[t]he peptide label is used as an affinity label for binding to chip-based antibody arrays" and then cites a number of references for methods of attaching peptide labels to oligonucleotides. Nowithstanding this, Iris *et al.* does not teach that the oligonucleotides encode the polypeptides. As noted above, the peptide tags disclosed by *Iris et al.* are chemically attached to the oligonucleotide probes, they are not encoded by the oligonucleotide probes. .

Therefore, Iris *et al.*, which does not disclose any combinations of containing a collection of capture agents that bind to preselected polypeptides and a collection of oligonucleotides , where each member of the collection of oligonucleotides contains a sequence of nucleotides E_m that encodes a preselected polypeptide, nor that all sets of capture agents specifically bind to different polypeptides encoded by the oligonucleotides, it does not

cure deficiencies in the teachings of Lerner *et al.*, which fails to teach or suggest any of the these elements. Therefore, the combination of teaching teachings of Lerner *et al.* and Iris *et al.*, does not result in the instantly claimed combinations and systems. Thus, the Examiner has failed to set forth a *prima facie* case of obviousness.

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In view of the above, consideration of the amendments and remarks herein and allowance of the application are respectfully requested.

Respectfully submitted,

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